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The management of adult psychiatric emergencies in low and middle income countries: a systematic review

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Abstract

Background

Mental health specialist services in low and middle income countries (LMIC) are scarce. The aim of this review was to identify effective interventions and treatment guidelines to manage common types of psychiatric emergencies in non-specialist settings in LMIC.

Methods

We conducted a systematic review of interventions for psychiatric emergencies and a literature search for LMIC-specific treatment guidelines for psychiatric emergencies.

Outcomes

We identified one randomised controlled trial from LMIC which indicated that a brief psychosocial intervention delivered to patients with attempted suicide/s resulted in significant reduction in completed suicide/s but not in repeated suicidal behaviour. We identified 22 treatment guidelines for psychiatric emergencies in LMIC, but only one was based on context-relevant evidence or developed following rigorous procedures. The guidelines included those on the 'neuroses' spectrum, externalising spectrum, suicidal behaviour and substance use related presentations. The most commonly covered phenotypes were alcohol intoxication (monitoring of vital signs, supportive interventions and symptomatic management), alcohol withdrawal (sedation, thiamine, symptomatic treatment), and suicidal behaviour (risk assessment, management of risk, referral to relevant specialists). None of the guidelines dealt with the issue of people with mental illness who are unable to consent to treatment.

Interpretation

There is a dearth of high quality guidelines and contextualised primary evidence for management of psychiatric emergencies in LMIC. This needs to be an urgent research priority given the adverse health and social consequences of such presentations and the current drive to scale-up mental health care.

Introduction

A psychiatric emergency is a severe disturbance of mood, thought, or behaviour that needs an immediate intervention.[1] A large proportion of people attending emergency services in High Income Countries (HIC) present with mental health problems requiring treatment. Indeed, in emergency services settings, psychiatric emergencies are reported to be as frequent as trauma-related and neurological emergencies, constituting up to 12% of emergency service attenders.[2] Common psychiatric disorders found in people presenting to emergency services in HIC include psychoses (12-29%), substance abuse disorders (6-25%), mood disorders (depression and bipolar disorders) (2-23%) and personality disorders (11-20%).[3-5] Furthermore, in HIC, people with depression, anxiety or substance use disorders are high users of emergency medical services.[6] Many common emergency presentations, such as attempted suicide and agitated or disturbed behaviour, cut across diagnostic categories.[7,8]

The vast majority of people with mental health problems living in low and middle income countries (LMIC) do not have access to treatments that are shown to be efficacious and cost-effective in such settings.[9-11] For this reason, emergency presentations are expected to be more frequent in these populations. Due to a variety of factors, including lack of availability of specialist services, people with mental health problems often make their first presentation to non-specialist settings.[12,13] Thus, the management of psychiatric emergencies is more likely to fall to non-specialists working in non-psychiatric settings, for example, primary care or general hospital emergency departments. Health professionals working in general health care settings in LMICs therefore need the necessary skills to handle psychiatric emergencies. An important resource that would help these health professionals are evidence-based guidelines which provide a framework for the management of psychiatric emergencies in a non-specialist, LMIC setting. While many such evidence-based guidelines have been developed in HIC[14-17], the generalisability of such guidelines to LMIC may be limited as LMIC may differ significantly with regard to characteristics of clinical phenotypes, the available human resources for delivering the intervention, available interventions, and mental health legislation with regards to involuntary treatment.

The aim of this review was two-fold, 1) To identify and evaluate the evidence base for the effectiveness of interventions for psychiatric emergencies in adults in non-specialist settings in LMIC; and 2) To review the availability, coverage, and quality of treatment guidelines for psychiatric emergencies in LMIC.

Methods

Systematic review of the literature

This systematic review was carried out in line with the PRISMA statement for reporting systematic reviews [18] and was guided by a review protocol.

Randomised and non-randomised controlled trials, observational studies, pilot studies, and case series were included if they were conducted in any setting except specialist mental health settings e.g. general hospitals, emergency departments, primary care and mental health services provided by Non-Governmental Organisations (NGO) in any LMIC as defined by the World Bank at the time that the study was carried out (http://data.worldbank.org/about/country-classifications/country-and-lending-groups). Interventions delivered in specialist psychiatric settings (e.g. psychiatric wards, psychiatric emergency departments) were excluded as the goal of the review was to examine interventions that could be delivered in non-specialist settings. Interventions delivered to children and adolescents or delivered in post-conflict or humanitarian settings were excluded as they address issues in specific patient groups and settings which have distinct requirements which are beyond the scope of this review.

The search took the approach of focusing on phenotypic presentations (for example, suicide attempts) as they are likely to have more relevance in non-specialist emergency settings. To ensure a comprehensive search of priority phenotypes, the search terms were informed by a survey of experts. A consensus list of phenotypic presentations was generated based on discussion among the author group. World Psychiatric Association (WPA) regional and country representatives and other key informants identified by the authors were contacted by e-mail and invited to respond to the survey (Appendix 1). Experts were asked to rate a list of phenotypic presentations (e.g. aggression/violence, mute/uncommunicative, self-harm, bizarre behaviour) on a three point Likert scale of 'extremely relevant', 'moderately relevant' and 'not relevant' for their context. They were also asked to suggest any other phenotypes which were relevant but not on our list. A total of 27 experts from 17 countries (Armenia, Bangladesh, Cambodia, Jordan, Kenya, Moldova, Mongolia, Niger, Sudan, Togo, Uganda, Ethiopia, Georgia, India, Pakistan, Egypt, and Nigeria) participated in the survey.

The following presentations were excluded: seizures, acute adverse effects of psychotropic medications, and acute behavioural disturbance due to delirium (as the most common aetiologies are not attributed to mental health problems). There were no limits to the delivery agent (e.g. general physician, nurse, mental health professional), type of intervention (e.g. psychosocial, pharmacological, environmental) and control groups (e.g. no treatment, alternative treatment). The detailed inclusion and exclusion criteria are presented in Appendix 2.

We searched the following databases with no restriction on date of publication: Medline, EMBASE, PsycINFO, CINAHL (Cumulative Index to Nursing and Allied Health Literature), Cochrane library,

Web of Knowledge, LILACS (Literatura Latino Americana em Ciências da Saúde) (comprehensive index of scientific and technical literature from Latin America and the Caribbean), Indmed (indexes peer reviewed medical journals published from India) and ELDIS (Electronic Development and Environment Information System). We searched title, abstract and key words under the following concepts: Mental disorder (e.g. schizophrenia, depression, mania), phenotype (e.g. aggression, bizarre behaviour), presentation (e.g. acute, emergency, crisis), management (e.g. treatment, intervention, therapy), type of country (e.g. developing, under developed, low income) and country (e.g. Bhutan, Sudan, Vietnam). The detailed search strategy is included in Appendix 3. The literature search was conducted by AN in October 2014. Titles and abstracts of all studies were double screened by AN and DF/UB to determine eligibility for full text screening. Disagreement about eligibility for inclusion in the review was resolved by discussion with RS and EK. Data were extracted independently by UB and CH using a data extraction form designed to achieve study objectives. The extracted data was then checked by AN for consistency and any gaps addressed. Data extracted included the following: country, study design, phenotype, diagnostic criteria, sampling strategy, sample size, intervention and intervention components, intervention agent and comparison group. We assessed the quality of the included RCTs using the Cochrane Risk of Bias tool to rate the RCTs on the following dimensions: allocation concealment, blinding of participants & personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias. The analyses plan was to do a meta-analyses if there were enough homogenous studies.

Guideline search

To retrieve relevant treatment guidelines, we invited key informants (described above) to identify guidelines for psychiatric emergencies which were developed or used in their country. In addition, RS, AN and EK conducted a search using Google Scholar with the following search terms: 'emergency psychiatric clinical guidelines' and 'acute psychiatric clinical guidelines'. CR, SP and SF conducted a search for relevant guidelines from Latin American countries and not published in English. An a priori decision was taken to include the World Health Organisation's mhGAP intervention guide for mental, neurological and substance use disorders [19] in the review as an example of high quality guidelines developed through a systematic process and designed for LMIC settings. [20] The quality of guidelines was assessed on three dimensions, namely 'treatment efficacy', 'clinical utility', and 'guideline development process' using the American Psychological Association 'Criteria for Evaluating Treatment Guidelines'.[21] Data from English language guidelines were extracted independently by UB and CH while data from non English guidelines were extracted by CR, SP and SF.

Results

a) *Systematic review*

The database search returned 16687 papers. After excluding duplicates and ineligible papers, we carried out full text evaluation of the remaining 23 papers. 21 papers were excluded as they did not describe evaluation of an intervention or were not based in a LMIC or were not conducted in non-specialist emergency settings (Fig 1). We were able to identify two papers, both evaluating the same intervention from the same study, the WHO Multisite Intervention Study on Suicidal Behaviours (SUPRE-MISS), a multi-country, individual RCT which evaluated a brief educational intervention and periodic follow-up contacts (BIC) for suicide attempters in India, Sri Lanka, Islamic Republic of Iran, People's Republic of China, and Brazil.[22,23] Consecutive suicide attempters (defined using ICD10 criteria) attending the emergency care departments were randomised to either BIC (n = 922) or treatment as usual (TAU) (n = 945). BIC was delivered by a person with clinical experience (e.g. doctor, nurse, psychologist) and included TAU plus a one-hour individual information session followed by nine follow-up contacts (phone calls or visits) over 18 months. The results showed that overall, at 18 months, significantly fewer deaths from suicide occurred in the BIC than in the TAU group (0.2% vs. 2.2%, $p< 0.001$).[23] However, there was no significant difference between the proportion of subjects with repeated suicide attempts in the BIC and TAU groups (7.6% vs. 7.5%).[22] Inadequate information was provided regarding variables like allocation concealment, blinding of personnel and blinding of outcome assessment, thus raising concerns about potential bias. However, there was considered to be a high risk of selection bias because of selective attrition from the intervention and comparison arms (Web table 1).

b) *Literature review of guidelines*

Through the grey literature search and key informants we identified twenty-one treatment guidelines (excluding the mhGAP-IG). We found one set of guidelines each from Thai-Burmese border,[24] Uganda,[25] South Africa (SA),[26] India,[27] Namibia,[28] Malawi,[29] Kiribati,[30] Ghana,[31] Kenya,[32] Zambia, [33] Ethiopia,[34] Vanuatu,[35] Afghanistan[36] and Colombia.[37] We found the maximum number of guidelines from Brazil (n=4), [38-41] followed by Peru (n=3).[42-44] The mhGAP-IG were developed for use across LMICs.[19] Two set of guidelines (including mhGAP) addressed a range of mental disorders,[19,36] while others were specific, for example on the management of opiate disorders,[27] crack disorders[38] or psychotic disorders[42]. One guideline was specific for the aggression and agitation phenotype[39]. The remaining guidelines addressed psychiatric emergencies alongside other medical emergencies.[24-26,28-35,37,40,41,43,44]

Web table 2 describes the quality criteria used to evaluate the guidelines and specifies which of the guidelines clearly fulfilled each of these criteria. A few claimed to be evidence based and/or based on WHO recommendations/other guidelines without specifying the approach followed to evaluate the literature.[25,26,33-35] None of the guidelines fulfilled all of the quality criteria but some [19,27,31,36] fulfilled many as summarised in web table 2. With a few exceptions[19,27,31,40] most of the guidelines did not

consider the level of methodological rigor and clinical sophistication of the evidence supporting the intervention proposed.

We organised the phenotypes under four broad groups: the 'neuroses' spectrum (e.g. acute anxiety, conversion), externalising symptoms (e.g. agitation, aggression), suicidal behaviour and substance use related presentations (e.g. opiate intoxication, alcohol withdrawal). Tables 1 to 4 present a summary of the recommendations derived from a synthesis of the recommendations from the various guidelines. Recommendations made in two or more guidelines are classified under 'common recommendations' and the rest are classified as 'other recommendations'.

Tables 1-4 here

For some phenotypes there were more than one set of guidelines recommending a common intervention (e.g. diazepam for alcohol withdrawal), while for other phenotypes only one set of guidelines recommended a particular intervention (e.g. diazepam for conversion symptoms). The most commonly addressed phenotypes were alcohol intoxication/withdrawal and suicidal behaviour. For alcohol intoxication, the 'common recommendations' were monitoring of vital signs, supportive interventions (e.g. lateral positioning, rehydration) and symptomatic management (e.g. management of hypoglycaemia). For alcohol withdrawal the 'common recommendations' included sedation using diazepam, prophylaxis against Wernicke Korsakoff syndrome using thiamine, multi vitamin supplementation, rehydration and symptomatic treatment (e.g. antipsychotics for psychotic symptoms, and benzodiazepines or anti-epileptics for withdrawal seizures). Finally, for suicidal behaviour the 'common recommendations' included detailed risk assessment, management of risk (e.g. treat underlying mental illness, liaise with support networks) and referral to specialist professionals as appropriate.

The management of other phenotypes were as follows. Clonazepam is recommended for acute anxiety. For agitation and aggression, recommendations included interventions that were verbal (e.g. de-escalation through firm but friendly communication), mechanical (e.g. physical restraint) and pharmacological (e.g. benzodiazepines like diazepam and anti-psychotics like haloperidol). Diazepam and clonidine were recommended for opioid withdrawal. For both crack/cocaine intoxication and amphetamine intoxication the principles of treatment were the same i.e. benzodiazepine for management of agitation, anti-psychotics for management of psychotic symptoms if any and monitoring of vital signs.

Discussion

The approach taken in this review to the problem of psychiatric emergencies was based on phenotypic presentations rather than on syndromal diagnoses. The rationale for this was that the immediate

management of psychiatric emergencies, particularly in non-specialist settings, requires treatment of the presenting symptoms that are causing distress, and that this is often distinct from the longer term management driven by the syndromal diagnosis. We found only one study empirically evaluating a treatment of a psychiatric emergency in a non-specialist settings in LMIC[22,23] which indicated that a brief psychosocial intervention delivered to patients with attempted suicide/s resulted in significant reduction in completed suicide/s[23] but not in repeated suicidal behaviour.[22] In addition, we were able to retrieve 22 treatment guidelines for psychiatric emergencies in LMIC,[24-44] however, only the WHO's mhGAP-IG[19] was based on context-relevant evidence or developed following rigorous procedures to ensure clinical utility.

Data from HIC indicate that there is an increasing trend of psychiatric emergencies presenting to general hospitals.[45] There is no evidence to suggest that this would be any different in LMIC, and indeed the burden might be higher on such services for a host of reasons. The shortage of specialist human resources in LMIC makes it imperative that non-specialist health service providers are adequately trained and equipped to deliver evidence based treatment guidelines. Experiences from HIC show that the use of short, focussed training programs for general health care professionals improves knowledge, diagnostic accuracy and treatment of psychiatric emergencies in non-specialist settings.[2,46-49] Such training needs to be supplemented by contextualised and evidence based guidelines to ensure sustained delivery of high quality care. However, our review found an almost complete absence of empirical evidence about management of psychiatric emergencies in non-specialist settings in LMIC. Furthermore, the few guidelines to manage psychiatric emergencies in LMIC had notable flaws in the methodology used for their development. The synthesis of recommendations from the guidelines and the RCT (Table 1) shows that, while there are treatment guidelines for some of the phenotypes (e.g. suicidality, alcohol withdrawal), many phenotypes are not represented at all (e.g. stupor, catatonia, mutism). The overall quality of the guidelines was weak and there was considerable variation in the recommendations for specific phenotypes, for example in terms of medications and dosages.

One of the APA criteria that we used to examine the guidelines was whether they considered patients' 'willingness and ability to participate in recommended interventions'. None of the guidelines included in our review fully met that criterion. This is a substantial shortcoming for guidelines that are to be used to treat psychiatric emergencies, as many of the patients might have reduced capacity to give informed consent for treatment. Hence, consideration of the legal provisions and protection provided in a specific country to patients with reduced capacity to consent is essential while drafting treatment guidelines. This is particularly important, in light of the observation made by the United Nations Committee on the Rights of Persons with Disabilities that laws authorising the involuntary treatment

on the basis of mental disability are non-compliant with the Convention on the Rights of Persons with Disabilities (CRPD).[50]

Our review shows that there is a lack of empirically based and contextually appropriate guidelines on how to manage psychiatric emergencies in non-specialist settings in LMIC. In the short term mental health systems could follow the recommendations synthesised in the guidelines reviewed in our paper, but ultimately should adapt these through rigorous guideline development processes. In addition, high-quality evidence from robust designs, ranging from clinical cohorts to randomised controlled trials of the management of psychiatric emergencies in specialist mental health settings in LMICs are essential to evaluate recommendations and novel approaches.

Guidelines for the management of psychiatric emergencies in non-specialist healthcare settings also need recommendations on the management of patients who have reduced capacity to consent which are compliant with both local laws and international conventions. One of the concerns about conducting trials in psychiatric emergencies is around ethical issues, in particular in relation to the involvement of patients with limited capacity. However, the TREC trials, which compared two drug treatments for people with aggression or agitation due to mental illness in LMIC, have demonstrated that rigorous yet pragmatic RCTs can be carried out in people presenting with psychiatric emergencies in middle-income country settings and provide a suitable model for future trials in non-specialist settings. [51]

The guidelines should be based primarily on a framework of contextually relevant phenotypic presentations with the goal of providing quick relief from distressing psychiatric phenomena. The guidelines should be graded according to their feasibility (for example, the cost of medications and competencies needed to deliver interventions) and acceptability (for example, the regulatory restrictions on their use in specific settings). While there are expected to be some contextual specificities, these are likely to be smaller than the universal principles of management of psychiatric emergencies and an mhGAP-IG styled set of guidelines may be an appropriate format for synthesis of these recommendations.

(Box 1 here)

Our review has several strengths. To the best of our knowledge, this is the first attempt to synthesize evidence on the types and management of psychiatric emergencies in non-specialist settings in LMIC. We have synthesised data from two sources, thereby increasing the generalizability of our findings. Although we have presented the synthesised recommendations we would like to specify that this is by no means an endorsement of the quality of the source guidelines and the synthesised

recommendations are only as good as the guidelines from which they are derived. Finally, we approached the problem using a phenotypic approach, on the grounds that this would be of more practical value to frontline health professionals, as compared to the conventional syndromal diagnosis approach adopted by mhGAP-IG. One limitation of our review is that our literature search was limited to the English language, although our guidelines search covered multiple languages. In addition, the summary treatment recommendations that we have presented are based on the synthesis of guidelines which are themselves limited by the weak quality of the evidence base and methodology of their development.

(Box 2 here)

In conclusion, there is a dearth of high quality guidelines and contextualised primary evidence for management of psychiatric emergencies in LMIC. Existing guidelines are restricted to a small number of emergency presentations, of uneven quality, and neglect to provide guidance regarding the management of people with reduced capacity to consent. Our review thus raises several pertinent questions which have major research and clinical implications. There is ample well-documented evidence on the assessment and management of psychiatric emergencies in non-specialist settings.[52] However, this evidence primarily comes from HIC which differ contextually from LMIC on various dimensions e.g. availability of trained human resources and medications. Given that much of the visible morbidity (and possibly mortality) associated with mental disorders is due to such presentations, our findings call for an urgent investment in the expansion of the evidence base for management of psychiatric emergencies in LMIC and the development of contextualised guidelines following a rigorous methodology.

Authors' contributions

1) Abhijit Nadkarni: Lead author co-ordinating review process, developed the search strategy, conducted database search, screened and selected studies, wrote the first draft of the paper and co-ordinated further drafts.

2) Daniela Fuhr: Helped develop search strategy and review protocol, independently screened search results for papers for full text screening, independently screened full text of papers for final inclusion, and commented on all drafts.

3) Rahul Shidhaye: Commented on search strategy and review protocol, independently conducted grey literature search, and commented on all drafts.

4) Charlotte Hanlon: Commented on search strategy and review protocol, independently conducted data extraction and commented on all drafts.

5) Urvita Bhatia: Independently screened search results for papers for full text screening, independently screened full text of papers for final inclusion, independently conducted data extraction, and commented on all drafts.

6) Eugene Kinyanda: Commented on search strategy and review protocol, conducted search of grey literature, and commented on all drafts.

7) Celina Ragoni: Searched for guidelines from Latin American countries and extracted data form such guidelines.

8) Sérgio Luiz de Azevedo Perocco: Searched for guidelines from Latin American countries and extracted data form such guidelines.

9) Sandra Fortes: Searched for guidelines from Latin American countries and extracted data form such guidelines.

10) Thara Rangaswamy: Commented on search strategy and review protocol, mentored the authors' group, and commented on all drafts.

11) Vikram Patel: Conceptualized the paper, commented on search strategy and review protocol, mentored the authors' group, and commented on all drafts.

All authors read and approved the final draft.

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Table 1: Summary of guidelines for the management of 'neuroses' spectrum emergencies in non-specialist settings in low and middle income countries

Phenotype	Recommendations	Source guideline/RCT from which recommendation is derived
Acute anxiety	*Common recommendations*:* Clonazepam 0.25- 0.5 sublingually. *Other recommendations*:* Diazepam 5-10 mg IV	Brazil[39] Peru[44]
Conversion	*Common recommendations:* None *Other recommendations:* Explanation. This must be clear and coherent. It must emphasize the genuineness of the condition that it is common, potentially reversible and does not mean that the sufferer is a psychotic. Treatment of comorbid depression or anxiety if present. Diazepam 5-10mg PO/IM/IV. Psychosocial intervention Refer to higher level for appropriate management.	Kenya[32] Afghanistan[36] Brazil[41]

* Common recommendations: Recommendations made in two or more guidelines; other recommendations: Recommendations made in only one guideline.

Cautionary note: The guidelines from which the information in this table has been derived are only as good as the evidence that has informed them and the guideline development process followed. Hence, this information should be used at the clinician's discretion and in the context of standard drug formulary recommendations about the various drug dosages.

Table 2: Summary of guidelines for the management of externalising spectrum emergencies in non-specialist settings in low and middle income countries

Phenotype	Recommendations	Source guideline/RCT from which recommendation is derived
Agitation, overactive, aggressive, violent, excitement	*Common recommendations:* Verbal de-escalation. Assess in pairs in calm settings, with or without family/friends. Keep lines of communication open by talking to the patient in a firm but friendly manner until the situation is under control. Diazepam 2-20 mg IV, 5-10 mg PO or 10 mg IM for acute agitation secondary to anxiety. Chlorpromazine 50−150 mg IM or 200 mg QID PO or 200 mg every two hours if very aggressive Haloperidol 5-10 mg IM Physical restraint, if used, should be temporary and in combination with sedation and close medical supervision. Restrain patient when necessary without causing injuries. Protect yourself, have enough people to handle patient, don't immediately remove physical restraints. *Other recommendations:* Risperidone 2mg and Clonazepam 2-4mg. Olanzapine 5 mg and Diazepam 10-20mg. Quetiapine 100-200mg. Haloperidol 5 mg IM + Chlorpromazine 25 mg IM to be repeated once after 1-2 hours if necessary. Patients >60 years: Haloperidol, 5−10 mg IV or 10−20 mg IM or Chlorpromazine 50−75 mg IM If no response with oral medications then use Lorazepam 2 – 4 mg IM with/without Haloperidol 5mg IM or Olanzapine 5 – 10mg IM or Clothiapine (max 360mg/24 hrs). If no response then use Diazepam 10 mg IV or zuclopenthixol acetate IM 50 – 150mg (only if detained under Mental Health Act). Refer to general hospital if hemo-dynamically unstable or organic etiology is suspected.	South Africa[26] Malawi[29] Ghana[31] Ethiopia[34] Vanuatu[35] Afghanistan[36] Peru[42,43]

Cautionary note: The guidelines from which the information in this table has been derived are only as good as the evidence that has informed them and the guideline development process followed. Hence, this information should be used at the clinician's discretion and in the context of standard drug formulary recommendations about the various drug dosages.

Table 3: Summary of guidelines for the management of suicidal behaviour in non-specialist settings in low and middle income countries

Phenotype	Recommendations	Source guideline/RCT from which recommendation is derived
Suicidal	*Common recommendations*	mhGAP[19]
	Detailed assessment and risk assessment. Talk with the patient and try to understand what is the actual problem and try to identify cause for suicidal behaviour	SUPRE-MISS RCT[22, 23]
	Treat an underlying mental illness such as a severe depression	Uganda[25]
	Liaise with relevant parties. Talk to important relatives or friends.	South Africa[26]
	If there is risk of harming again, ask relatives to spend time with him and ensure that she/he is not left alone. Do not leave them alone. Carefully observe patient to minimize risk of self-harm.	Malawi[29]
		Kenya[32]
	Refer to relevant professionals	Vanuatu[35]
	Consider the need to hospitalise and hospitalise unless properly supervised at home	Afghanistan[36]
	Other recommendations	
	Brief Intervention and Contact (BIC): Individual information session (information about suicidal behaviour as a sign of psychological and/or social distress, risk and protective factors, basic epidemiology, repetition, alternatives to suicidal behaviours, and referral options) before discharge followed by nine follow-up contacts (phone calls or visits).	
	Form a contract with the patient	
	Provide emergency contacts	
	Provide adequate psychological care	
	Refer or call a pastor	

Cautionary note: The guidelines from which the information in this table has been derived are only as good as the evidence that has informed them and the guideline development process followed. Hence, this information should be used at the clinician's discretion and in the context of standard drug formulary recommendations about the various drug dosages.

Table 4: Summary of guidelines for the management of and substance use related emergency presentations in non-specialist settings in low and middle income countries

Phenotype	Recommendations	Source guideline/RCT from which recommendation is derived
Opiate intoxication	*Common recommendations*: None *Other recommendations*: Naloxone 0.4 mg IV. If no response within 2 minutes, repeat 0.4-0.8 mg twice more at 5-minute interval. If antidote for opiate overdose is not available treatment is symptomatic- analgesia and sedation	mhGAP[19] Thai Burmese border[24] India[27]
Opiate Withdrawal	*Common recommendations*: Diazepam 10 mg orally of 10mg intravenously as a starting dose, repeat every hour until sedation. Clonidine 0.15 mg orally as starting dose daily for 10 days. *Other recommendations:* Behaviour tending towards assault: Haloperidol 5-10 mg PO TDS or Chlorpromazine 50-100 mg PO TDS. Pain: Paracetamol 1 gm PO every three hours as necessary. Referral to substance treatment centre Treat with reducing doses of opioids (methadone, buprenorphine) or alpha-adrenergic agents (lofexidine) using either supervised dosing or daily dispensing. Treat specific symptoms as needed (diarrhoea, vomiting, muscle pain, insomnia). Consider starting opioid agonist maintenance treatment. Oral or i.v. rehydration, if necessary.	mhGAP[19] Thai Burmese border[24] Kenya[32] Afghanistan[36]
Amphetamine intoxication	*Common recommendations*: Give diazepam in titrated doses until the person is calm and lightly sedated. If psychotic symptoms do not respond to benzodiazepines, then consider using short-term antipsychotics. Monitor blood pressure, pulse rate, respiratory rate, and temperature every 2 – 4 hours. *Other recommendations:* Chlorpromazine 25-50mg IM rapidly reverses the acute agitation. Ammonium chloride 500mg PO every 4 hours.	mhGAP[19] Thai Burmese border[24] Colombia[37]
Crack intoxication	*Common recommendations*: Diazepam fractionated doses until tranquilization and mild sedation. Psychotic symptoms: Short-acting antipsychotics. Monitor vital signs every 2 hours. *Other recommendations:* Watch out for suicidal thoughts. Refer to hospital if chest pain, arrhythmia, violent or aggressive behaviour.	Colombia[37] Brazil[38]

Crack withdrawal	Maintain hydration. Avoid physical restraint. Anxiety or restlessness: Diazepam 5-40 mg. Motor agitation or psychotic symptoms: Haloperidol IM or Midazolam IM.	Brazil[38]
Cannabis intoxication	Maintain hydration Tranquilization with Midazolam 5mg IM	Colombia[37]
Alcohol intoxication	*Common recommendations* Gastric lavage if alcohol consumed within past two hours Position the patient in a lateral position because of possible vomiting and aspiration of vomit. Monitor clinical state and level of consciousness. Check urine output and vital signs every hour initially. Look for and treat hypoglycaemia. 50% Dextrose 20 ml IV bolus then 5% IV infusion. Rehydrate with iv saline when unconscious, then by mouth when able to swallow safely Supportive interventions Refer to next level hospital if no improvement. *Other recommendations* If signs of encephalopathy, give Thiamine 100mg IV/IM If agitated or violent: Diazepam 10 mg IV, repeat if needed after 30 minutes.	mhGAP[19] Thai Burmese border[24] South Africa[26] Namibia[28] Malawi[29]
Alcohol withdrawal	*Common recommendations* May need admission to hospital. Monitor clinical status including glucose levels, and intervene as indicated Thiamine 50-500 mg. PO daily or Thiamine 100-400 mg daily, IM (3-5 days) then PO Multi vitamin tablets, Vit B Co tablets daily, Vitamin B12, Folic Acid Rehydrate orally and intravenously (Sodium Chloride 0.9% in 5% Glucose) as required. For psychotic symptom use haloperidol 0·5–5 mg three times a day orally or intramuscularly, or 5−10 mg intravenously once a day, or 2–10 mg intramuscularly; or use chlorpromazine 25–50 mg intramuscularly 1–3 times a day, or 100–300 mg orally four times a day Withdrawal seizures: Phenytoin IV 10-15 mg/kg, diazepam IV Prophylaxis for withdrawal seizures: Diazepam or Carbamazepine 600-800 mg/day for 48 hours then taper by 200 mg/day. Diazepam (PO or IV): Various regimens Aggressive/Restless: Lorazepam 2-4mg 8hourly IM. Diazepam 10-15 mg IV or 10 mg IM or Lorazepam 2-4 mg PO. 50 ml of 50% dextrose for hypoglycaemia. *Other recommendations* Aggressiveness: Haloperidol 5 mg IV every 20-30 minutes until patient is calm then 5mg IV 4-8 hours depending on condition or Hydroxyzine 50-100 mg PO stat, then every 4-6 hours. High blood pressure: Clonidine.	mhGAP[19] Thai Burmese border[24] South Africa[26] Namibia[28] Malawi[29] Kiribati[30] Ghana[31] Kenya[32] Colombia[37] Brazil[39,40]

	Manage head trauma and treat pneumonia. Phenytoin, oral, 100 mg 3 times daily for 5 days may be used if seizures persist and are not controlled by Diazepam alone. Seclusion and restraints as necessary.	

Cautionary note: The guidelines from which the information in this table has been derived are only as good as the evidence that has informed them and the guideline development process followed. Hence, this information should be used at the clinician's discretion and in the context of standard drug formulary recommendations about the various drug dosages.

Box 1 Recommendations for the management of psychiatric emergencies in non-specialist settings in LMIC

-Guidelines to be developed immediately based on the best available global evidence.

-Guideline development should follow a rigorous process like those recommended by the Grading of Recommendations Assessment, Development and Evaluation (short GRADE) Working Group.

-Treatment recommendations should be for phenotypic presentations.

-Guidelines should have clear recommendations on management of patients without capacity to consent.

-LMICs should generate high quality primary evidence which will address gaps in the evidence and enable the continuing evaluation and refinement of contextualised guidelines.

Box 2 Research in context

Review

We conducted a systematic review of interventions for psychiatric emergencies and a search of LMIC specific treatment guidelines for psychiatric emergencies. Findings were then synthesised qualitatively to achieve study objectives.

Interpretation

There is a dearth of high quality guidelines and contextualised primary evidence for management of psychiatric emergencies in LMIC. There is an urgent need for the expansion of the evidence base and the development of contextualised guidelines following a rigorous methodology.

WEB EXTRA MATERIAL

Web Table 1: Quality of RCT included in the review

CITATION (AUTHOR, YEAR)	RANDOM SEQUENCE GENERATION	ALLOCATION CONCEALMENT	BLINDING OF PARTICIPANTS & PERSONNEL	BLINDING OF OUTCOME ASSESSMENT	INCOMPLETE OUTCOME DATA	SELECTIVE REPORTING	OTHER BIAS
Fleishmann et al. 2008[22]; Bertolete et al. 2010[23]	Low risk.	Unclear risk. Papers mention that the allocation sequence was kept in a separate location but do not give information about the safeguards to concealment.	Unclear risk. Participants were blinded but no information provided about blinding of investigators	Unclear risk. Papers don't provide any information.	High risk. Selective attrition from the intervention and comparison arms.	Not apparent	Not apparent

Web Table 2: Quality of guidelines

Domain	Criteria	Clearly fulfilled
TREATMENT EFFICACY	Take into consideration the level of methodological rigor and clinical sophistication of the research supporting the intervention.	mhGAP,[19] India,[27] Ghana,[31] Brazil[38]
	Consider clinical opinion, observation, and consensus among recognized experts representing the range of views in the field	mhGAP,[19] Ghana,[31] Zambia,[33] Colombia,[37] Brazil[38-41]
	Systematized clinical observation is weighted more heavily than un-systematized observation in evaluating treatment efficacy.	Colombia,[37] Brazil[38], Peru[42-44]
	The evaluation of treatment efficacy places greatest emphasis on evidence derived from sophisticated empirical methodologies	mhGAP,[19] India,[27] Ghana[31]
	Recommendations take into consideration the treatment conditions to which the intervention has been compared	mhGAP,[19] India[27]
	Consider whether the treatment gets better results than doing nothing.	mhGAP,[19] India[27]
	Consider whether the intervention offers the patient any benefit beyond simply being in treatment.	mhGAP,[19] India[27]
	Consider whether an intervention's results are better than the results of other interventions	mhGAP,[19] India[27]
	Consider available evidence regarding patient-treatment matching.	South Africa,[26] Namibia[28]
	Specify the outcomes the intervention is intended to produce	mhGAP,[19] India,[27] Ghana[31]
CLINICAL UTILITY	Reflect the breadth of patient variables that may influence the clinical utility of the intervention	mhGAP,[19] India,[27] Malawi,[29] Ghana,[31] Zambia,[33] Ethiopia,[34] Brazil[40]
	Take into account the complexity and idiosyncrasy of patients' clinical presentations	mhGAP,[19] South Africa,[26] India,[27] Malawi,[29] Zambia,[33] Afghanistan,[36] Brazil,[38-41]
	Take into consideration culturally relevant	mhGAP,[19] India,[27] Vanuatu,[35]

	research and expertise	Afghanistan[36]
	Take into consideration research addressing the issue of the patient's gender	mhGAP,[19] Afghanistan[36]
	Take into account research concerning the age and developmental level of the patient	mhGAP,[19] South Africa,[26] India,[27] Malawi,[29] Ghana,[31] Zambia,[33] Ethiopia,[34] Colombia,[37] Peru,[42-44]
	Take into account research and clinical consensus on other relevant patient characteristics	mhGAP,[19] ndia,[27] Malawi[29]
	Take into account data on how differences between individual health care professionals may affect the efficacy of the treatment.	None
	Take into account the effect of the health care professional's training, skill, and experience on treatment outcome	Kenya,[32] Afghanistan[36]
	Take into account the effects on treatment outcome of interactions between the patient's and the health care professional's characteristics	Afghanistan[36]
	Take into account information pertaining to the setting in which the treatment is offered.	Thai-Burmese border,[24] Uganda,[25] India,[27] Namibia,[28] Kenya, [32] Vanuatu[35], Afghanistan,[36] Brazil[39]
	Take into account data on treatment robustness.	mhGAP,[19] India,[27] Ghana,[31]
	Take into account the intervention's level of acceptability to the patients	India,[27] Malawi,[29] Vanuatu, [35]
	Provide for informed patient choice among comparable interventions.	mhGAP,[19] India,[27] Vanuatu[35]
	Consider patients' willingness and ability to participate in recommended interventions.	Brazil[38]
	Explicitly note and evaluate possible adverse effects of interventions	mhGAP,[19] Thai Burmese border,[24] Uganda,[25] India,[27] Namibia,[28] Malawi,[29] Ghana,[31] Zambia,[33] Ethiopia,[34] Brazil[38,39]
	Address the preparation of the health care professionals to deliver the intervention.	mhGAP,[19] Uganda[25]
	Costs should be reported separately from	None

	consideration of effectiveness.	
	Should consider the direct, indirect, short-term, and long-term costs to the patient, to the professional, and to the health care system	None
GUIDELINE DEVELOPMENT	Composed of individuals with a broad range of documented expertise.	mhGAP,[19] Ghana,[31] Zambia,[33] Colombia,[37] Brazil[38,40,41]
	Include one or more individuals with expertise in the delivery of services	mhGAP,[19] Thai Burmese border,[24] Uganda,[25] South Africa,[26] India,[27] Namibia,[28] Kiribati,[30] Ghana,[31] Kenya,[32] Zambia,[33] Ethiopia,[34] Vanuatu,[35] Afghanistan,[36]Colombia,[37] Brazil[38-41], Peru[42-44]
	Include one or more individuals with expertise in the scientific methodology of intervention evaluation	mhGAP,[19] South Africa,[26] Ghana,[31] Afghanistan,[36] Colombia,[37] Brazil[38-41]
	Include representatives of the patient community	mhGAP,[19]
	Include experts from a broad range of relevant disciplines	mhGAP,[19] Namibia,[28] Zambia,[33] Brazil[41]
	Include members with expertise and sensitivity to relevant issues of diversity	mhGAP,[19]
	Panel members should disclose potential, actual, and apparent conflicts of interest.	mhGAP,[19] Ghana,[31]
	Panels should maintain the climate of openness and free exchange of views	Brazil[41]
	Selection criteria for guideline panellists/qualifications/potential conflicts of interest should be described	Brazil[41]
	Panel procedures and deliberations be made available for review by concerned parties.	None
	Before being adopted, the guidelines be widely distributed to concerned parties and resulting comments be considered	mhGAP,[19] Uganda,[25] Kenya[32]
	Reference list of reviewed in developing the guidelines be included with the guidelines	mhGAP,[19] India,[27] Brazil[38-41]

	Any disagreements between panel members be noted in the guidelines.	Brazil[41]
	Guideline panels agree on specific goals for constructing the guidelines.	mhGAP,[19] Uganda,[25] India,[27] Namibia,[28] Malawi,[29] Ghana,[31] Kenya,[32] Vanuatu,[35] Afghanistan,[36] Colombia,[37] Brazil[40-41], Peru[42-44]
	Guideline panels identify the audience for whom the guideline is intended.	mhGAP,[19] Uganda,[25] South Africa,[26] India,[27] Namibia,[28] Malawi,[29] Kenya,[32] Ethiopia,[34] Brazil[39-41]
	Goals of guideline development should be clearly identified in the guidelines.	Uganda,[25] Kenya,[32] Brazil[39,41]
	Guideline panel define the process and methods of guideline development	mhGAP,[19] Brazil[41]
	Guideline panel specify the target condition for the treatments under consideration.	mhGAP,[19] Thai-Burmese border,[24] Uganda,[25] South Africa,[26] India,[27] Namibia,[28] Malawi,[29] Ghana,[31] Kenya,[32] Zambia,[33] Ethiopia,[34] Vanuatu,[35] Afghanistan,[36] Colombia,[37] Brazil[38-41], Peru[42-44]
	Guideline panel specify the patient population(s) for whom the treatments under consideration are intended.	mhGAP,[19] Thai-Burmese border,[24] Uganda,[25] South Africa,[26] India,[27] Namibia,[28] Malawi,[29] Ghana,[31] Kenya,[32] Zambia,[33] Ethiopia,[34] Vanuatu,[35] Afghanistan,[36] Brazil[38-40], Peru[42-44]
	Guideline panel specify what clinical interventions will and will not be considered.	mhGAP,[19] Brazil[38]
	Guideline panel specify the type of professional and the practice setting to which the guideline will be applicable.	mhGAP,[19] South Africa,[26] Namibia,[28] Ghana,[31] Kenya,[32] Ethiopia,[34] Vanuatu,[35] Afghanistan,[36], Brazil[39]
	Guideline panel decide on specific subsidiary goals around which literature reviews will be organized.	mhGAP,[19] Brazil[41]
	Guideline panels should specify the methods used for reviewing evidence.	mhGAP,[19] Brazil[41]

	Guideline panels specify methods for evaluating the guidelines they produce.	mhGAP,[19] Uganda,[25] Brazil[41]
	Guideline panels make detailed recommendations to facilitate independent evaluation of the reliability of the guidelines	Brazil[41]
	Guideline panels make detailed recommendations to facilitate independent evaluation of the validity of the guidelines	None
	Guideline panels make detailed recommendations to facilitate independent evaluation of the clinical utility of the guidelines	Uganda[25]
	Guidelines be reviewed and revised periodically	mhGAP,[19] Uganda,[25] Malawi,[29] Kenya,[32] Zambia,[33] Ethiopia,[34] Brazil[41]

Appendix 1

QUESTIONNAIRE ON THE DIAGNOSIS AND MANAGEMENT OF PSYCHIATRIC EMERGENCIES IN LOW RESOURCE SETTINGS

1. Listed below are the common psychiatric phenotypic presentations seen in emergency settings. Kindly rate (✓) each one on the scale for relevance in your country/regional setting.

Phenotype	Extremely relevant	Moderately relevant	Not relevant
Extreme sadness			
Aggression/ Violence			
Agitation			
Mute/uncommunicative			
Self harm without suicidal intent			
Suicidal			
Confusion			
Bizarre			

behaviour

Dissociative amnesia or fugue

Catatonia

Substance intoxication

Substance withdrawal

Sudden medically unexplained loss of function

Medically unexplained seizures

Stupor

Trance/possession

2. Please record any other common phenotypic presentations (apart from the ones above) that are relevant in your country/regional settings.

3. Please recommend any relevant diagnostic/treatment guidelines for psychiatric emergencies from your country/region which we can cite and use for our review. Please send us these guidelines as an attachment or indicate from where we can obtain them.

Please email the completed questionnaire and soft copies of diagnostic/treatment guidelines to abhijit.nadkarni@lshtm.ac.uk

Appendix 2

Inclusion and exclusion criteria

	Included	**Excluded**
Publication type	• Any date • English language (manuscript to specify how many had to be excluded because of language)	
Study design	• Individual RCTs • Cluster RCTs • Individual non-randomised trials / evaluative studies • Individual observational studies including case series Pilot studies	Case reports
Countries	All Low and Middle Income Countries (LMIC) as per world bank list of economies 2013	High Income Countries (HIC)
Settings	• General hospital • Accident & Emergency • Primary care • NGOs	Specialist psychiatric settings
Population	• Adult patients (18 years and above) with a target psychiatric disorder or phenotypic presentation (defined below) • All genders	Children and adolescents
Psychiatric phenotypic presentations	• Aggressive/agitated behaviour • Uncommunicative behaviour • Acute distress • Sudden loss of bodily function (functional) • Self-harm/suicidal behaviour • Bizarre behaviour	• Epilepsy/organic seizures • Acute adverse effects of psychotropic medications e.g. dystonia, lithium toxicity • Delirium
Psychiatric disorder	• Conversion disorder • Panic disorder • Panic attack	

	• Anxiety • Schizophrenia • Psychosis • Psychoses • Psychotic • Mania • Manic • Hypomania • Hypomanic • Bipolar affective disorder • BPAD • Manic depressive psychoses • Brief psychotic episode • Acute and transient psychotic disorder • Acute stress reaction • Adjustment disorder • Intoxication • Withdrawal	
Intervention	Any intervention designed specifically to treat the presenting problem (e.g. pharmacological agent, psychological therapy).	
Control group (If applicable)	Any comparison group including: • Placebo (for drug trials) and treatment as usual (for psychotherapy trials). • Trials which compare the effectiveness of two active interventions for example comparing drug vs. drug	

Appendix 3 Medline search strategy

1. Schizophrenia/
2. Psychosis/
3. Psychoses/
4. Mania/
5. Hypomania/
6. Bipolar affective disorder/
7. BPAD/
8. Manic depressive psychosis/
9. Manic depressive psychoses/
10. Brief psychotic episode/
11. Acute and transient psychotic disorder/
12. Acute stress reaction/
13. Adjustment disorder/
14. Or 1-13
15. Schizophreni$.tw
16. Psycho$.tw
17. Mani$.tw
18. Hypomani$.tw
19. Bipolar affective disorder.tw
20. BPAD.tw
21. Manic depressive psychos$.tw
22. Brief psychotic episode.tw
23. Acute and transient psychotic disorder.tw
24. Acute stress reaction.tw
25. Adjustment disorder.tw
26. Or 15-25
27. Aggress$.tw
28. Violen$.tw
29. Agitat$.tw
30. Mut$.tw
31. Uncommunicative.tw
32. Distress$.tw
33. Self harm$.tw
34. Self-harm$.tw
35. Overdose.tw
36. Suicid$.tw
37. Parasuicide.tw
38. Confus$.tw
39. Bizarre.tw

40. Amnesi$.tw
41. Fugue.tw
42. Catatoni$.tw
43. Dissociati$.tw
44. Intoxicat$.tw
45. Withdrawal.tw
46. Conversion .tw
47. Stupor$.tw
48. Trance.tw
49. Possession.tw
50. Hysteri$.tw
51. Panic.tw
52. Anxiety.tw
53. Or 27-52
54. 14 or 26 or 53
55. Acute
56. Emergency
57. Crisis
58. Or 55-57
59. Treatment/
60. Intervention/
61. Management/
62. Therapy/
63. Diagnosis/
64. Or 59-63
65. Treat$.tw
66. Intervention.tw
67. Management.tw
68. Therapy.tw
69. Diagnosis.tw
70. Or 65-69
71. 64 or 70
72. Developing.tw
73. Less$ developed.tw
74. Under developed.tw
75. Underdeveloped.tw
76. middle income.tw
77. low income.tw
78. lower income.tw
79. low and middle income.tw

80. lmic.tw
81. lmics.tw
82. lamics.tw
83. lamic.tw
84. third world.tw
85. lami countr$.tw
86. Transitional countr$.tw
87. Or 72-86
88. Afghanistan
89. Armenia$
90. Bangladesh
91. Benin
92. Bhutan
93. Bolivia
94. Burkina Faso
95. Burkina Fasso
96. Upper Volta
97. Burundi
98. Urundi
99. Cambodia
100. Khmer Republic
101. Kampuchea
102. Cameroon$
103. Cameron$
104. Cape Verde
105. Central African Republic
106. Chad
107. Comoros
108. Comoro Islands
109. Comores
110. Congo
111. Zaire
112. Cote d Ivoire
113. Ivory Coast
114. Djibouti
115. French Somaliland
116. East Timor
117. East Timur
118. Timor Leste
119. Egypt

120. El Salvador
121. Eritrea
122. Ethiopia
123. Gambia
124. Gaza
125. Georgia$ Republic
126. Ghana
127. Guatemala
128. Guinea
129. Guinea-Bisau
130. Guiana
131. Guyana
132. Haiti
133. Honduras
134. India
135. Indonesia
136. Kenya
137. Kiribati
138. Korea
139. Kosovo
140. Kyrgyz$
141. Kirghiz$
142. Kirgizstan
143. Lao PDR
144. Laos
145. Lesotho
146. Basutoland
147. Liberia
148. Madagasca$
149. Malagasy
150. Malawi
151. Nyasaland
152. Mali
153. Mauritania
154. Micronesia
155. Moldov$
156. Mongolia
157. Morocco
158. Ifni
159. Mozambique

160. Myanma$
161. Burma
162. Nepal
163. Antilles
164. Nicaragua
165. Niger$
166. Pakistan
167. Papua New Guinea
168. Palestine
169. Paraguay
170. Philippines
171. Philipines
172. Phillipines
173. Phillippines
174. Rwanda
175. Ruanda
176. Samoa$
177. Navigator Islands
178. Sao Tome
179. Senegal
180. Sierra Leone
181. Sri Lanka
182. Ceylon
183. Solomon Islands
184. Somali$
185. Sudan
186. Swaziland
187. Syria$
188. Tajikistan
189. Tadzhikistan
190. Tadjikistan
191. Tadzhik
192. Tanzania
193. Togo$
194. Uganda
195. Ukraine
196. Uzbek$
197. Vanuatu
198. New Hebrides
199. Vietnam

200. Viet Nam
201. West Bank
202. Yemen
203. Zambia
204. Zimbabwe
205. Rhodesia
206. Angola
207. Fiji
208. Palau
209. Albania
210. Gabon
211. Panama
212. Algeria
213. Grenada
214. Peru
215. American Samoa
216. Hungary
217. Romania
218. Argentina
219. Iran
220. Serbia
221. Azerbaijan
222. Iraq
223. Seychelles
224. Belarus
225. Jamaica
226. South Africa
227. Belize
228. Jordan
229. St. Lucia
230. Bosnia and Herzegovina
231. Kazakhstan
232. St. Vincent and the Grenadines
233. Botswana
234. Lebanon
235. Suriname
236. Brazil
237. Libya
238. Thailand
239. Bulgaria

240. Macedonia,
241. Tonga
242. China
243. Malaysia
244. Tunisia
245. Colombia
246. Maldives
247. Turkey
248. Costa Rica
249. Marshall Islands
250. Turkmenistan
251. Cuba
252. Mauritius
253. Tuvalu
254. Dominica
255. Mexico
256. Venezuela
257. Dominican Republic
258. Montenegro
259. Ecuador
260. Namibia
261. Or 88-260
262. 87 or 261
263. 54 AND 58 AND 71 AND 262